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ORIGINAL RESEARCH

Low NAPR as a Novel Indicator for Predicting *Escherichia coli* Bloodstream Infection and Improved Prognostic Outcomes in Elderly Hospitalized Inpatients: A 12-years Retrospective Cohort Study

Xinjie Han[1–3,*], Yang Yang[4,*], Jianbo Zhong[2,5,*], Zhenghao Yu[1,2], Pinzheng Zhang[5], Xinran Liu[2,5], Yongkai Ding[2,5], Qi Zhang[6], Pingjun Zhu[4], Guogang Xu[1], Yingzhen Du[2,5,7]

[1]Health Management Institute, The Second Medical Center and National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing, 100853, People's Republic of China; [2]Chinese PLA General Hospital, Medical School of Chinese PLA, Beijing, 100853, People's Republic of China; [3]Department of Respiratory and Critical Care Medicine, The Eighth Medical Center, Chinese PLA General Hospital, Beijing, 100853, People's Republic of China; [4]Department of Respiratory and Critical Care Medicine, The Second Medical Center and National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing, 100853, People's Republic of China; [5]Department of Disease Prevention and Control, The Second Medical Center and National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing, 100853, People's Republic of China; [6]The Second Medical Center and National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing, 100853, People's Republic of China; [7]Fever Clinic, The Second Medical Center and National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing, 100853, People's Republic of China

*These authors contributed equally to this work

Correspondence: Guogang Xu; Yingzhen Du, Email gxu@301hospital.org; zhenzhen52@163.com

Background: Bloodstream infections (BSIs) are associated with significant mortality, particularly in elderly patients. *Escherichia coli (E.coli*) is the most common causative organism in BSIs, but non-*E.coli* BSIs are associated with increased morbidity and mortality. Predictive biomarkers including the neutrophil-to-platelet ratio (NPAR) have not been well studied in elderly hospitalized patients. Our study aimed to compare the mortality in patients with *E.coli* and non-*E.coli* BSIs and, evaluate NPAR as a potential predictive biomarker for *E.coli* infection in extremely elderly inpatients.

Methods: A single-center, retrospective cohort study was conducted, involving 510 elderly patients diagnosed with bloodstream infections. Patients were divided into two groups based on the pathogen responsible for the infection: *E.coli* (n=92) and non-*E.coli* (n=418). Clinical data, comorbidities, and laboratory parameters were systematically collected. Kaplan-Meier survival analysis and Cox proportional hazards models were used to assess mortality risk, adjusting for relevant confounding variables. The predictive value of NPAR for *E.coli* bloodstream infection was analyzed via odds ratios (OR) and trend tests. Microbiological analysis of blood samples was performed according to the Clinical and Laboratory Standards Institute protocols.

Results: Non-*E.coli* BSIs was associated with greater mortality compared to *E.coli* BSI; hazard ratio (HR)=0.43 (95% CI=0.21, 0.88; *P*=0.021). NPAR was a significant predictor of *E.coli* BSI; for continuous NPAR, the odds of *E.coli* BSI decreased by 12% per unit increase in NPAR (OR=0.88; 95% CI=0.84, 0.93; *P*<0.001). The odds ratio of the lowest tertile of NPAR versus rest was 0.21 (95% CI=0.11, 0.40, *P*<0.001).

Conclusion: Non-*E.coli* BSIs are associated with greater mortality in elderly patients, while low NPAR is strongly associated with *E.coli* BSI. These findings suggest that NPAR may be useful for early risk stratification and clinical management of elderly patients with BSIs.

Keywords: bloodstream infection (BSI), *Escherichia coli*, neutrophil-to-platelet ratio (NPAR), elderly, retrospective cohort study

Introduction

Bloodstream infections (BSIs) are a major global health problem in the elderly as age-related immune defects, multiple comorbid conditions and diminished physiological reserves predispose these patients to high morbidity, prolonged

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hospitalization and increased mortality.[1,2] Although *Escherichia coli* (*E.coli*) is the predominant pathogen causing BSIs, non-*E.coli* organisms such as *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* associated with BSIs are known to be more severe, and result in higher mortality and complex treatment requirements necessitating a longer hospital stay.[3] The elderly are at particular risk for complicated clinical courses due to late diagnosis which may limit prompt initiation of appropriate treatment, thereby emphasizing the need for pathogen-specific risk stratification approach.

Neutrophil-to-platelet ratio (NPAR) also reflects both systemic inflammation and thrombotic risk.[4] Elevated NPAR is associated with poor prognosis in sepsis and other bacterial infections, but the role of NPAR in predicting *E.coli* bloodstream infection (BSI) among elderly patients was not well studied.[5] With development of microfluidics and novel phage-based detection systems, combining NPAR with pathogen specific diagnostic tools holds promise in the early management of *E.coli* BSI. Though evidence suggests that patients experience higher mortality in non-*E.coli* compared to *E.coli* infection causing BSIs, there is currently no study that has directly compared risk of mortality between *E.coli* and non- *E.coli* BSIs among elderly population. Furthermore, the utility of NPAR in predicting *E.coli* BSI among elderly patients remains unexplored.

This study aimed to compare mortality between *E.coli* versus non-*E.coli* BSIs among elderly inpatients, explore potential utility of NPAR as a diagnostic biomarker to predict *E.coli* BSI and its prognostic implications among them.

Methods

Study Design and Participants

This single-center, retrospective cohort study encompassed 527 elderly patients diagnosed with BSIs between December 2011 and February 2024 at the Second Medical Center of the Chinese PLA General Hospital through the hospital's infection information system. The inclusion criteria were: (1) age greater than 65 years; and (2) availability of complete medical records. The exclusion criteria were as follows: (1) Incomplete medical records. The study protocol was reviewed and approved by the Chinese PLA Hospital Ethical Committee (Approval No.NO. S2024-359-02) and complied with the Declaration of Helsinki. Due to the retrospective design, informed consent was waived.

Data Collection

Data on NPAR levels and other covariates, including demographic and clinical factors, were collected at baseline. NPAR was measured as both a continuous variable and categorized into tertiles (T1, T2, and T3). The outcome of interest was the occurrence of *E.coli* BSI, which was confirmed by blood culture. A BACT/ALERT 3D automatic blood culture instrument (bioMérieux, France) was used for blood culture, a Vitek2 Compact automatic microbiological identification and antimicrobial susceptibility analysis system (bioMérieux, France) was used for strain identification and antimicrobial susceptibility testing. Baseline data were collected on a range of demographic and clinical characteristics, including age, gender, department, smoking status, comorbidities (eg, diabetes mellitus, hypertension, coronary disease), and clinical interventions (eg, number of operations, use of ventilator, central venous catheter, urinary catheter, chemotherapy, radiotherapy, blood transfusion, polypharmacy regimens). The hospitalization duration was also recorded as a continuous variable.

Statistical Analysis

Descriptive statistics were used to summarize the baseline characteristics of the participants. Continuous variables were expressed as means with standard deviations, and categorical variables were reported as frequencies and percentages. Categorical variables were compared using the chi-square or Fisher's exact test; continuous variables were analyzed using the Student's *t*-test, Mann–Whitney *U*-test or Kruskal–Wallis test as appropriate; logistic regression was used to assess the predictive value of NPAR for *E. coli* BSI; Cox proportional hazards models were applied for survival analysis; and the Kaplan–Meier method with Log rank test was used to compare mortality between groups. To evaluate the association between NPAR and *E. coli* BSI, we constructed three models in our analysis: Model 1: Unadjusted crude model. Model 2: Adjusted for age and sex. Model 3: Based on Model 2, we further adjusted for variables that showed statistical significance in the univariate analysis, as well as through reverse adjustment, including department, coronary disease, and combination of drug. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for both

continuous NPAR and NPAR tertiles (T1 as the reference group). The dose-response relationship for continuous NPAR was assessed, and the trend across NPAR tertiles was evaluated using a likelihood ratio test. The non-linearity of the dose-response relationship was examined using a non-linear regression model. The p-value for trend was calculated to assess the monotonicity of the dose-response across tertiles of NPAR. Statistical significance was set at $P < 0.05$ for all analyses. All statistical analyses were performed using R (version 3.6.3) statistical software.

Results

Baseline Characteristics

A cohort of 510 elderly participants (mean age 89.9 ± 8.5 years) meeting inclusion and exclusion criteria was stratified into *E. coli* BSI (n=92, 18.2%) and non-*E.coli* BSIs groups (n=418, 81.8%) based on the causative agent of bloodstream infection. The baseline characteristics of the overall cohort and the two groups are summarized in Table 1. No intergroup differences in age (*P*=0.978), gender (*P*=0.229), smoking status (*P*=0.193), diabetes (*P*=0.614), or hypertension (*P*=1.0). Higher coronary disease prevalence in non-*E.coli* group (57.2% vs 32.3%, *P*<0.001) and comparable surgical frequency (*P*=0.441).

Clinical Interventions and Outcomes

As shown in Table 2, 49.1% (n = 510) patients did not require ventilator support, with a higher proportion of patients in the *E. coli* group (61.3%) compared to the non-*E.coli* group (46.4%) (*P* = 0.045). Similarly, the duration of central

Table 1 Baseline Clinical Characteristic of Enrolled Bloodstream Infection Patients

Characteristic	Overall (n = 510)	*Escherichia coli* Group (n = 92)	Non-*Escherichia coli* Group (n = 418)	*P* value
Age, year (mean±SD)	89.9±8.5	90.0±9.3	89.9±8.3	0.978
Gender, n (%)				
Female	15 (2.9)	5 (5.4)	10 (2.4)	0.229
Male	495 (97.1)	87 (94.6)	408 (97.6)	
Department, n (%)				
Internal medicine	460 (90.0)	77 (83.7)	382 (91.4)	0.046
Surgery	51 (10.0)	15 (16.3)	36 (8.6)	
Smoking, n (%)				
No	313 (61.3)	63 (67.7)	250 (59.8)	0.193
Yes	197 (38.7)	29 (32.3)	168 (40.2)	
Diabetes, n (%)				
No	293 (57.3)	56 (60.2)	237 (56.7)	0.614
Yes	217 (42.7)	36 (39.8)	181 (43.3)	
Hypertension, n (%)				
No	122 (24.1)	21 (23.7)	101 (24.2)	1
Yes	388 (75.9)	71 (76.3)	317 (75.8)	
Coronary disease, n (%)				
No	241 (47.4)	62 (67.7)	179 (42.8)	<0.001
Yes	269 (52.6)	30 (32.3)	239 (57.2)	
Number of operations, n (%)				
0	332 (65.0)	65 (69.9)	267 (63.9)	0.441
1	111 (21.7)	19 (20.4)	92 (22.0)	
≥2	67 (13.3)	8 (9.7)	59 (14.1)	
Chemotherapy or radiotherapy, n (%)				
No	458 (89.6)	84 (90.3)	374 (89.5)	0.956
Yes	52 (10.4)	8 (9.7)	44 (10.5)	
Combination of drug, n (%)				
No	71 (13.9)	30 (32.3)	41 (9.8)	<0.001
Yes	439 (86.1)	62 (67.7)	377 (90.2)	

Table 2 Clinical Interventions and Outcomes of Enrolled Bloodstream Infection Patients

Characteristic	Overall (n = 510)	*Escherichia coli* Group (n = 92)	Non-*Escherichia coli* Group (n = 418)	*P* value
Days of ventilator, n (%)				
0	250 (49.1)	56 (61.3)	194 (46.4)	0.045
1-30	58 (11.4)	6 (6.5)	52 (12.4)	
31-90	106 (20.7)	18 (19.4)	88 (21.1)	
>90	96 (18.8)	12 (12.9)	84 (20.1)	
Days of central venous catheter, n (%)				
0	83 (16.2)	24 (25.8)	59 (14.1)	0.023
1-60	127 (24.9)	25 (26.9)	102 (24.4)	
61-90	136 (26.8)	17 (19.4)	119 (28.5)	
>90	164 (32.1)	26 (28.0)	138 (33.0)	
Days of urinary catheter, n (%)				
0	188 (37.0)	36 (39.8)	152 (36.4)	0.927
1-60	97 (19.0)	16 (17.2)	81 (19.4)	
61-90	89 (17.4)	16 (17.2)	73 (17.5)	
>90	136 (26.6)	24 (25.8)	112 (26.8)	
Blood transfusion, n (%)				
No	310 (60.9)	67 (73.1)	243 (58.1)	0.01
Yes	200 (39.1)	25 (26.9)	175 (41.9)	
Length of hospital stay (median [IQR])	90.0 (65.4, 96.0)	90.5 (75.2, 95.0)	90.0 (64.0, 96.0)	0.563

venous catheter use was significantly longer in the *E.coli* group, with 25.8% of patients requiring it for more than 90 days, compared to 14.1% in the non-*E.coli* group ($P = 0.023$). Blood transfusion was more frequently administered in the *E.coli* group (73.1% vs 58.1%, $P = 0.01$). The length of hospital stay did not differ significantly between the two groups ($P = 0.563$), with a median length of stay of 90.0 days (IQR: 65.4, 96.0) in the overall cohort.

Departments and Infection Source Distribution

There was a statistically significant difference between *E.coli* group and non-*E.coli* groups regarding the departments in which patients were hospitalized ($P = 0.046$) (Table 1). The distribution of departments of patients with *E.coli* bloodstream infections were as follows: Cardiology (16.30%), Endocrinology (3.26%), Gastroenterology (35.87%), Hematology (1.09%), ICU (4.35%), Nephrology (4.35%), Neurology (5.43%), Oncology (2.17%), and Respiratory Medicine (10.87%) (Figure 1). The distribution of infection sources among patients with *E.coli* bloodstream infections were as follows: Biliary infection source (28.26%), non-biliary intra-abdominal infection (3.26%), Pulmonary infection source (16.30%), Unidentified infection source (23.92%), and Urinary tract infection source (28.26%) (Figure 1). Also, we found that non-*E. coli* pathogens were the primary contributors. Among these, *Staphylococcus species* were the most prevalent, accounting for 125 isolates out of 510 total samples (Supplementary Table 1).

NPAR Associations with *E.coli* BSI

The association between NPAR and *E.coli* BSI was evaluated using three models (Table 3). All models demonstrated a statistically significant inverse relationship between continuous NPAR and *E.coli* BSI risk: Model 1, OR=0.88 (95% CI: 0.84, 0.93; $P < 0.001$), Model 2, OR =0.88 (95% CI: 0.84, 0.92; $P < 0.001$), and in Model 3, OR=0.89 (95% CI: 0.84, 0.94; $P < 0.001$). Using Tertile 1 (T1) as the reference group, in Tertile 2 (T2), the odds of infection were significantly reduced, with Model 1(OR=0.53; 95% CI: 0.32, 0.89; $P = 0.017$), Model 2(OR= 0.50; 95% CI: 0.29, 0.84; $P = 0.01$) and Model 3(OR =0.46; 95% CI: 0.26, 0.81; $P = 0.008$). In Tertile 3 (T3), the odds of infection were even more substantially reduced, with Model 1 (OR =0.21; 95% CI: 0.11, 0.40; $P < 0.001$), Model 2 (OR=0.21; 95% CI: 0.11, 0.39; $P < 0.001$), and Model 3 (OR= 0.23; 95% CI: 0.11, 0.46; $P < 0.001$). Furthermore, a statistically significant trend towards decreasing odds of infection across increasing tertiles of NPAR was observed in all models (P for trend < 0.001). These findings suggest that higher NPAR levels correlate

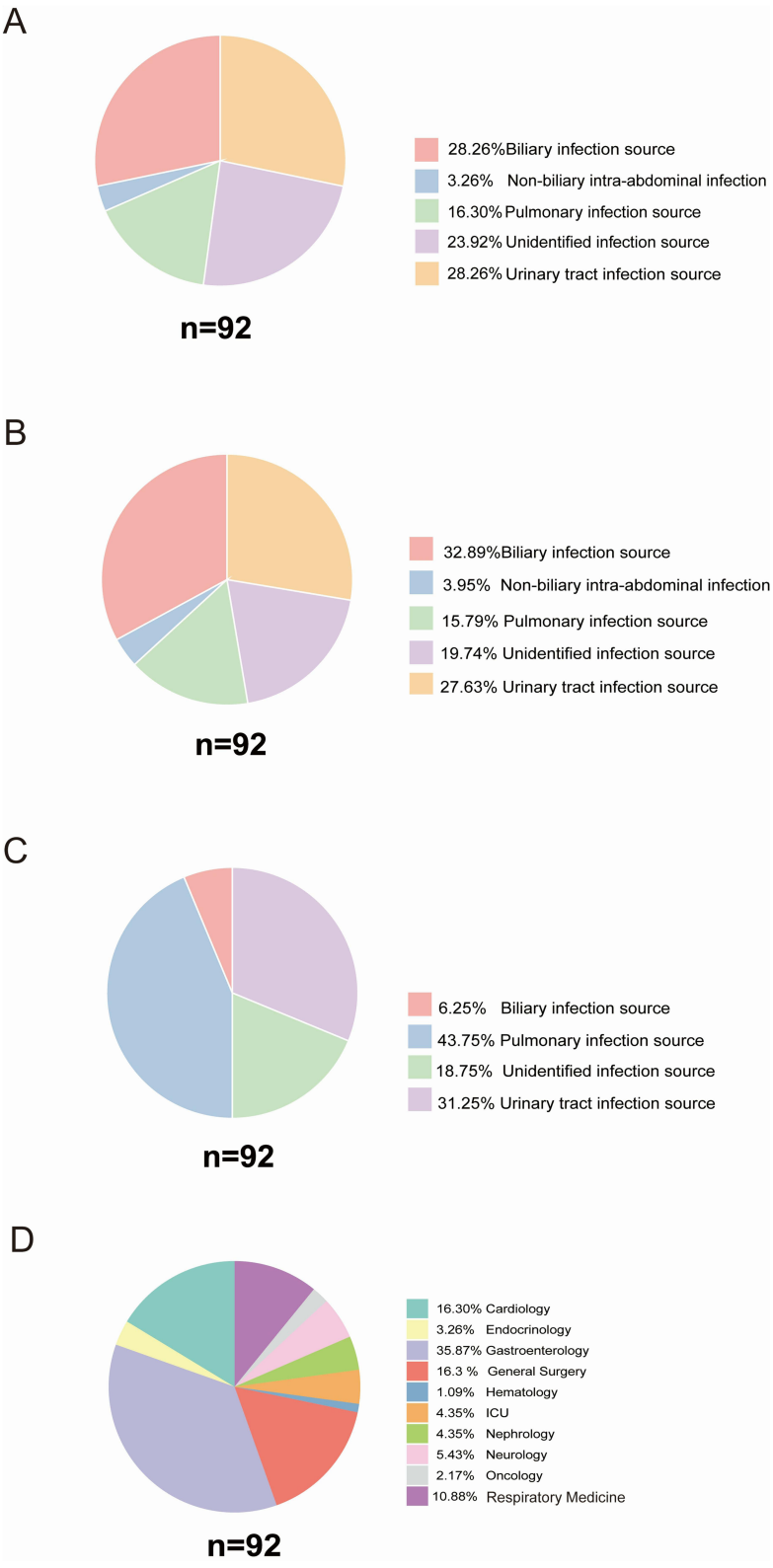

Figure 1 Distribution of infection sources and departments in patients with *Escherichia coli* bloodstream infections. (**A**) Distribution of infection sources in patients with *Escherichia coli* bloodstream infections. (**B**) Distribution of infection sources in internal medicine bloodstream Infection patients with *Escherichia coli*. (**C**) Distribution of infection sources in surgeon bloodstream infection patients with *Escherichia coli*. (**D**) Distribution of departments of patients with *Escherichia coli* bloodstream infections.

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Table 3 Associations of NPAR with *Escherichia coli* Bloodstream Infections in Elder Patients

	Model 1		Model 2		Model 3	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
NPAR (continuous)	0.88 (0.84, 0.93)	<0.001	0.88 (0.84, 0.92)	<0.001	0.89 (0.84, 0.94)	<0.001
NPAR (tertiles)						
T1	Reference		Reference		Reference	
T2	0.53 (0.32, 0.89)	0.017	0.5 (0.29, 0.84)	0.01	0.46 (0.26, 0.81)	0.008
T3	0.21 (0.11, 0.40)	<0.001	0.21 (0.11, 0.39)	<0.001	0.23 (0.11, 0.46)	<0.001
P for trend	<0.001		<0.001		<0.001	

Abbreviations: NAPR, neutrophil-to-platelet ratio; OR, Odds ratio.

with a reduced likelihood of *E.coli* BSI, with the risk decreasing progressively across tertiles. This aligns with NPAR's role as a composite inflammatory marker, where elevated values may reflect an attenuated susceptibility to systemic infection.

Dose-Response Relationship Between NPAR and *E.coli* BSI

A linear relationship between NPAR and *E.coli* BSI was statistically significant ($P < 0.05$), while a non-linear relationship was not evident ($P = 0.424$, Cutoff value =19.4) (Figure 2). Therefore, as NPAR increases, there is a linear decrease in *E.coli* BSI risk. Hence NPAR may serve as a continuous protective marker rather than having a threshold at a particular level.

Survival Analysis

The Kaplan-Meier survival plots of patients with *E.coli* and non-*E.coli* BSIs are shown in Figure 3, which revealed higher survival probability of patients with *E coli* compared with non-*E coli* counterparts (HR=0.43; 95% CI 0.21, 0.88, *P*=0.021). Notably, the survival probability for patients with non-*E.coli* infections dropped more rapidly over time, whereas the *E.coli* group exhibited a more gradual decline in survival.

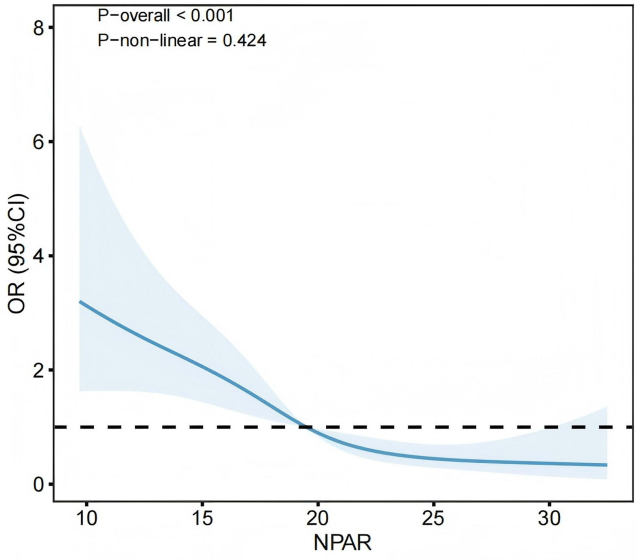

Figure 2 The dose-response relationship between NPAR and *Escherichia coli* bloodstream infection. (NAPR: neutrophil-to-platelet ratio).

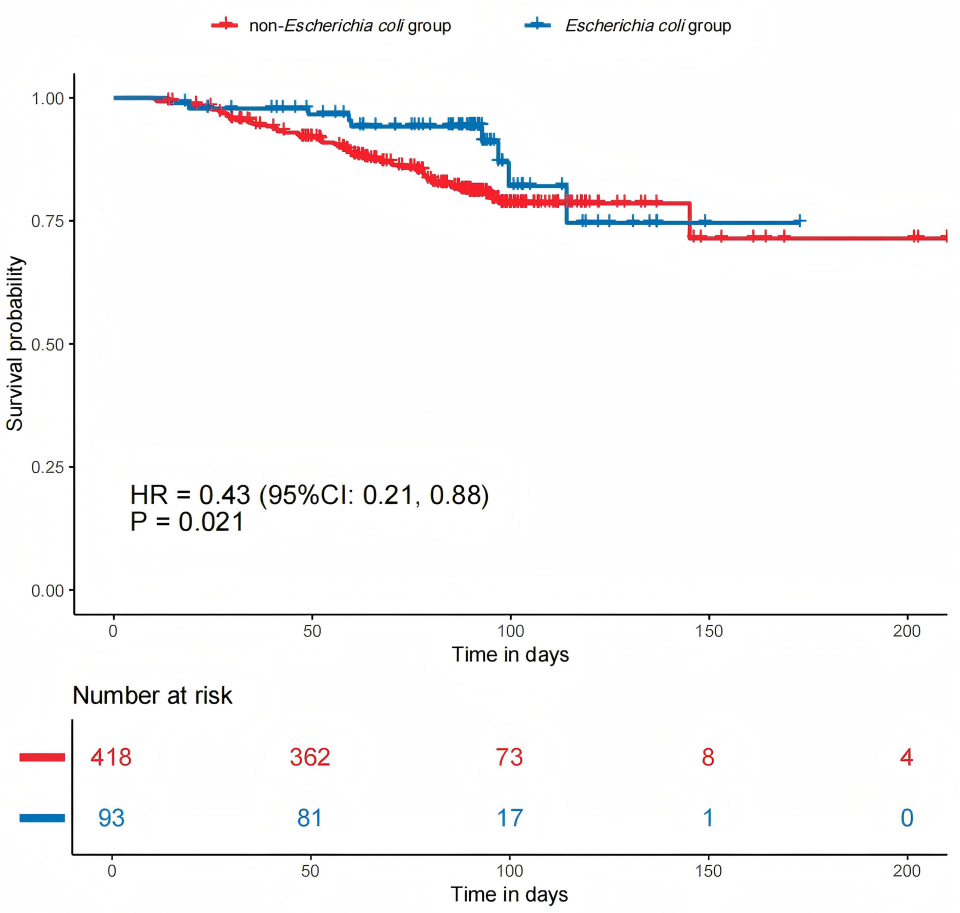

Figure 3 Kaplan-Meier curve analysis of patients in *Escherichia coli* and non-*Escherichia coli* bloodstream infection groups.

Antimicrobial Resistance Pattern

As shown in Table 4 and Figure 4, almost 97.1% of *E.coli* isolates were resistant to Ampicillin (AMP), 77.1% were resistant to Ciprofloxacin (CIP), 74.3% were resistant to Cefazolin (CEZ), 72.9% were resistant to Levofloxacin (LVX), and 72.7% were resistant to Ampicillin/Sulbactam (AMP/SUL). Overall, *E.coli* isolates exhibited no resistance to the following antibiotics: Amikacin (AMK), Ertapenem (ETP), Tigecycline (TGC), and Cefotetan (CET). The antibiotic with the highest resistance rate in *E.coli* isolates from bloodstream infection patients in the respiratory department were AMP (100%), Ceftriaxone (CTX, 100%), CEZ (100%). AMP (100%), Doxycycline (DXY, 100%), Gentamicin (GEN, 100%). In contrast, the general surgery department had a lower resistance rate for antibiotics like Ampicillin/Sulbactam (60.0%) and Gentamicin (66.7%). Notably, antibiotics like Amikacin, Ertapenem, and Tigecycline showed a resistance rate of 0% across all departments. Resistance to Cefotetan was absent across all departments tested.

Discussion

Our study provides several important implications to be addressed clinically for BSIs in extremely elderly patients. First, we demonstrated that non-*E. coli* BSIs had a significantly higher risk of mortality compared to *E. coli* BSI in extremely elderly inpatients with the mean age of 89.9 ± 8.5 years, indicating the clinical importance of identifying the pathogen causing infection. We also provided that low NPAR was inversely associated with the presence of *E. coli* BSI which may be useful early identification and risk stratification in elderly, leading to a more tailored and early intervention to be initiated.

Among 30,923 cases of *E.coli* bloodstream infections, 2961 cases of 30-day mortality were observed, resulting in an overall 30-day mortality of 9.6% (2961/30,923).[6] Hospital-acquired or third-generation-cephalosporin-resistant *E.coli* BSI showed significantly higher mortality rates compared to community-acquired or third-generation-cephalosporin-

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Table 4 Antibiotic Resistance Rate of *Escherichia coli* in Bloodstream Infection Patients

	Overall		Respiratory Medicine		Endocrinology		General Surgery		Neurology		Gastroenterology		Cardiology	
	R(%)	Total	R(%)	Total	R(%)	Total	R(%)	Total	R(%)	Total	R(%)	Total	R(%)	Total
Amikacin (AMK)	0	70	0	10	0	3	0	9	0	4	0	25	0	12
Ampicillin (AMP)	97.1	34	100	6	100	1	100	5	100	2	90.9	11	100	4
Ampicillin/Sulbactam (AMP/SUL)	72.7	33	83.9	6	100	1	60	5	0	2	80	10	100	4
Aztreonam (AZT)	41.1	70	40	10	66.7	3	44.4	9	25	4	52	25	25	12
Doxycycline (DXY)	34.4	32	50	4	100	2	66.7	3	0	1	15.4	13	42.9	7
Ertapenem (ETP)	0	32	0	6	0	1	0	5	0	2	0	9	0	4
Nitrofurantoin (NFT)	11.8	32	16.7	6	0	1	0	5	0	2	27.3	11	0	4
Cotrimoxazole (TMP/SMX)	37.1	70	60	10	33.3	3	77.8	9	50	4	20	25	25	12
Ciprofloxacin (CIP)	77.1	70	90	10	66.7	3	55.6	9	75	4	80	25	83.3	12
Meropenem (MEM)	11.1	36	25	4	0	2	25	4	75	4	14.3	14	0	8
Minocycline (MIN)	25.7	35	25	4	50	2	66.7	3	0	2	21.4	14	25	8
Piperacillin/Tazobactam (PIP/TAZ)	11.6	69	10	10	0	3	22.2	9	0	2	12.5	24	0	12
Gentamicin (GEN)	45.9	37	33.3	6	100	1	66.7	6	25	4	33.3	12	75	4
Tigecycline (TGC)	0	33	0	4	0	2	0	3	0	3	0	13	0	8
Ticarcillin/Clavulanate (TIC/CLA)	18.8	32	25	4	50	2	66.7	3	0	1	7.7	13	0	7
Cefoperazone (CFP)	35.6	59	44.4	9	33.3	3	42.9	7	0	1	24.2	18	18.2	11
Cefoperazone/Sulbactam (CFP/SUL)	20	35	25	4	50	2	25	4	25	4	15.4	13	12.5	8
Ceftriaxone (CTX)	64.7	34	100	6	100	1	60	5	0	2	63.6	11	75	4
Ceftazidime (CAZ)	31.9	69	30	10	33.3	3	50	8	25	4	36	25	25	12
Cefotetan (CET)	0	34	0	5	0	1	0	5	0	2	0	11	0	5
Cefazolin (CEZ)	74.3	35	100	5	100	1	60	5	50	2	72.7	11	100	6
Tobramycin (TOB)	6.2	65	10	10	0	3	0	8	0	3	4.3	23	0	11
Imipenem/Cilastatin (IPM/CS)	5.9	68	10	10	0	3	12.5	8	0	4	8.3	24	0	12
Levofloxacin (LVX)	72.9	70	80	10	66.7	3	44.4	9	75	4	4	25	83.3	12

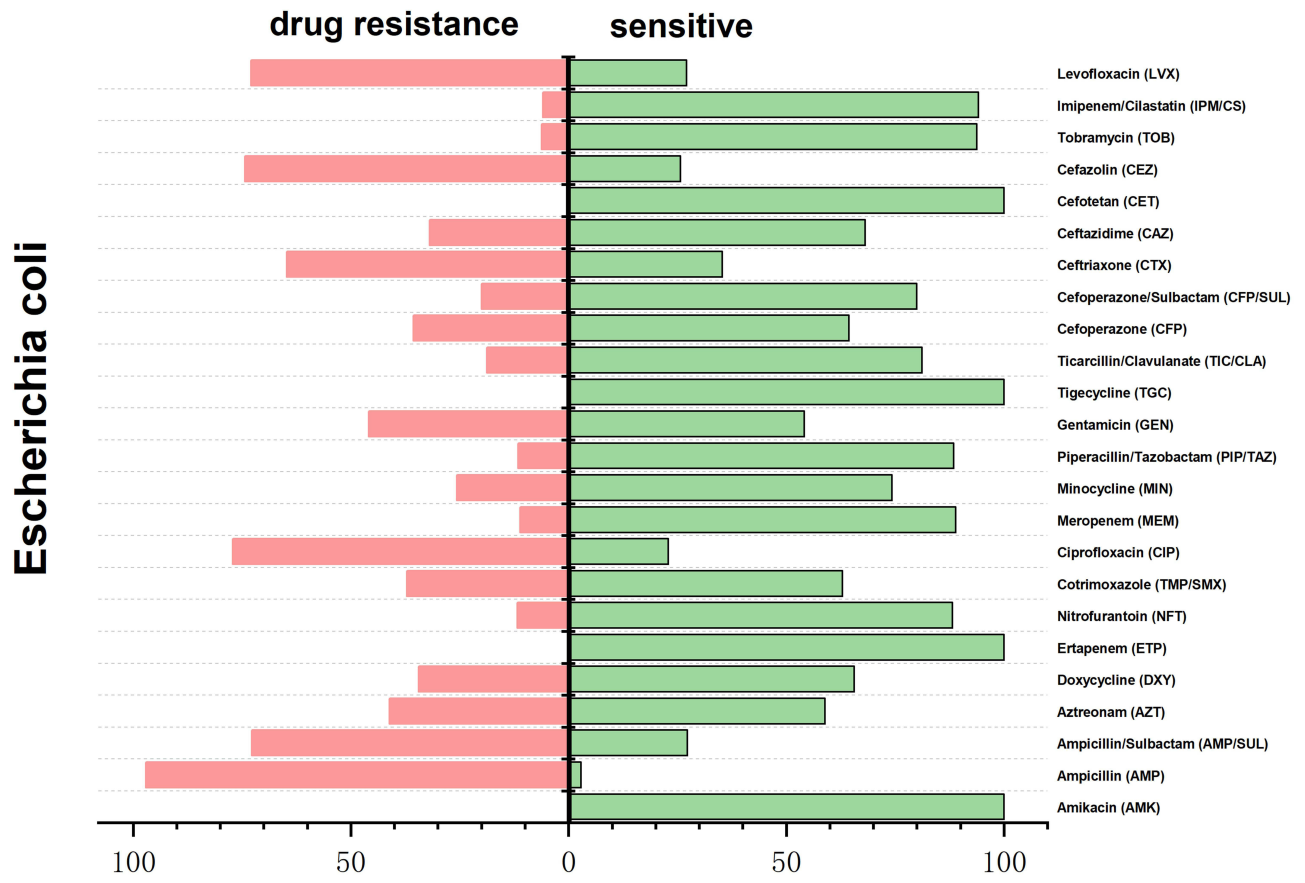

Figure 4 Overall antibiotic resistance rate of *Escherichia coli*.

susceptible *E.coli* BSI.[6] In our cohort of elderly patients, non-*E.coli* BSIs were associated with higher mortality compared to E.coli BSIs, even after adjustment for demographics and clinical factors, which is consistent with previous studies. Various studies have reported that the reasons why high mortality is associated with non-*E.coli* infections include difficulty in diagnosis, limited treatment options, and increased infection severity due to multidrug-resistant organisms or high virulence.[6,7] As elderly patients have weak immunity and often suffer from multiple underlying diseases, there would be a greater concern about their course and response to treatment.[8,9] Our findings indicate that it is vital to early detection and proper management for non-*E.coli* BSIs. Previous studies have reported that *E.coli* BSI in elderly patients predominantly originate from urinary tract infections,[10] which is consistent with the findings of our study, where urinary and biliary tract infections were identified as the leading sources. These infections typically elicit a relatively mild systemic inflammatory response, characterized by only a modest elevation in neutrophil counts and minimal alterations in platelet levels. In contrast, non-*E. coli* BSIs - such as those caused by *Staphylococcus aureus, Klebsiella pneumoniae*, or *Enterococcus faecalis* - are more often associated with catheter-related infections, non-biliary intra-abdominal infections, and respiratory tract infections, which usually trigger a more severe systemic inflammatory response.[11] It is reported that thrombocytopenia was independently associated with mortality among patients with BSIs.[12] This aligns with prior studies showing NPAR and related indices (eg, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio) as strong, independent predictors of sepsis severity and mortality.[13] A high NPAR captures a dual-risk profile: amplified inflammatory response and impaired hemostatic balance, both of which have been independently linked to increased mortality in bloodstream infections.[14] In our multivariable Cox regression models, high NPAR remained significantly associated with mortality even after adjusting for age, comorbidities, and infection source, indicating its robust prognostic value. Clinically, low NPAR may serve as an early indicator of *E. coli* BSI and help clinicians stratify patients who are likely to have more benign infection courses,

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potentially guiding early empirical therapy decisions and resource allocation. Conversely, persistently elevated NPAR should prompt vigilance for non-*E. coli* pathogens or complicated infection sources.

The prevalence of *E.coli* producing extended-spectrum beta-lactamases (ESBL) among BSI patients was 40.98%. *E. coli* isolates were generally sensitive to carbapenems and β-lactam/β-lactamase inhibitor combinations. Hospital-acquired infections, biliary tract infections, gastric tube insertion procedures, and prior cephalosporin administration were identified as independent risk factors for the isolation of ESBL-producing strains. ESBL positivity, hospital-acquired infections, and cancer were independent risk factors for mortality.[15] Meta-analysis results indicate that it is necessary to shift current treatment practices from antibiotic escalation strategies that delay appropriate therapy to early, relatively aggressive, and comprehensive antibiotic treatment, especially in patients with BSIs caused by *Klebsiella pneumoniae* or *E.coli*.[16] Choi et al found that *E.coli* is the most common pathogenic microorganism in BSIs, accounting for 32.3%, and the adjusted hazard ratio (aHR) for 30-day mortality and subsequent medical costs for *E.coli* BSI was lower compared to other microorganisms causing BSI. *E.coli*-BSI resulted in lower mortality rates during the first 7 days and from days 8 to 30 compared to BSIs caused by other microorganisms.[17] Our study found that the proportion of internal medicine patients was higher in the non-*E.coli* group, while *E.coli* infections were more common in the surgical department. The incidence of coronary artery disease was lower in the *E.coli* group, whereas it was higher in the non-*E.coli* group. There were significant differences in the duration of ventilator use and central venous catheter use between the *E.coli* and non-*E.coli* groups, with patients in the non-*E.coli* group having a longer durations of use.

NPAR is a simple, readily accessible measure derived from routine blood tests, and it has been proposed as a marker for various infectious and inflammatory conditions.[18–20] As shown in Figure 2, the OR for *E.coli* BSI decreases with increasing NPAR values. The analysis indicates a significant overall association between NPAR and the risk of *E.coli* bloodstream infection. Overall *P*-value: <0.001, indicating a strong statistical significance for the association between NPAR and the risk of *E.coli* bloodstream infection. In our analysis, the non-linear regression yielded a p-value of 0.424, indicating no significant evidence of a non-linear relationship between NPAR and infection risk. Therefore, we conclude that the relationship is best modeled as linear, suggesting a consistent, proportional association between NPAR and infection risk. OR (95% CI): The odds ratio decreases progressively with higher NPAR levels, approaching 1, indicating that higher NPAR values are associated with a reduced risk of *E.coli* bloodstream infection. Our findings suggest that low NPAR values are strongly associated with an increased risk of *E.coli* infection, with patients in the lowest NPAR tertile having substantially higher odds of having an *E.coli* infection compared to those in the highest tertile. This association remained consistent across various analytical models, further reinforcing the evidence for NPAR as a predictor of *E.coli* infections. Although the precise mechanisms linking NPAR to infection risk are not fully understood, it is believed that NPAR reflects the balance between inflammatory and immune responses.[21–23] During *E. coli* BSI, lipopolysaccharides (LPS) derived from the bacterial cell wall activate macrophages and other immune cells via Toll-like receptor 4 (TLR4) and related signaling pathways.[24] This activation triggers a cascade release of proinflammatory cytokines, including interleukin (IL)-6, IL-1, and TNF-α. Among these, IL-6 plays a central role in the IL-6–liver axis by markedly stimulating hepatic synthesis of thrombopoietin (TPO), the key regulator of megakaryocyte proliferation and differentiation.[25] Elevated TPO levels subsequently enhance platelet production, resulting in reactive thrombocytosis.[25] In addition, several inflammatory cytokines, such as IL-6, IL-11, and granulocyte-macrophage colony-stimulating factor (GM-CSF), may directly or indirectly act on hematopoietic stem and progenitor cells to promote megakaryocyte maturation and platelet release. In contrast, non-*E. coli* BSIs like *S. aureus* can induce platelet aggregation and clearance through α-toxin- and ClfA-mediated mechanisms, thereby promoting thrombocytopenia and contributing to an elevated NPAR.[26] Together, these inflammatory responses provide a plausible explanation for the increased platelet counts frequently observed in *E. coli* BSI and may partially underlie the association between a low NPAR and disease progression.

The antibiotic resistance profiles of *E.coli* isolates in this study reveal significant variability across different clinical departments. High resistance rates to Ampicillin, Ampicillin/Sulbactam, and Cefazolin are consistent with previous reports of widespread beta-lactam resistance.[27,28] However, the absence of resistance to Amikacin and Ertapenem is encouraging, as these antibiotics are vital for treating multidrug-resistant infections. The elevated resistance rates to Ciprofloxacin and Levofloxacin in the respiratory and cardiology departments may be linked to the frequent use of these antibiotics in those specialties. The lack of resistance to Tigecycline and Ertapenem across all departments

suggests that these antibiotics could serve as effective treatment options for *E.coli* bloodstream infections. The relatively low resistance rates to Imipenem/Cilastatin and Meropenem in most departments further highlight the importance of carbapenems in managing severe *E.coli* infections. The significant resistance to Ticarcillin/Clavulanate, particularly in the general surgery department, underscores the need for more judicious use of this antibiotic to prevent the development of further resistance. Doctors should emphasize careful monitoring of antibiotic use, restricting the use of broad-spectrum antibiotics, and promoting individualized treatment guided by sensitivity testing to reduce the spread of resistance.[29,30]

Conclusion

The NPAR, as demonstrated in our study, holds significant potential as a simple, cost-effective, and globally applicable biomarker for early identifying and targeted managing *E. coli* BSI in elderly patients. Low NPAR is associated with an increased likelihood of *E. coli* BSI and can help clinicians identify high-risk patients who may benefit from early therapeutic interventions. In future research, the role of NPAR as a predictive and prognostic biomarker for *E.coli* BSI could be further extended to populations across different age groups, with subsequent studies needed to explore longitudinal NPAR trends during treatment as a monitoring biomarker, and further elucidate the underlying biological mechanisms linking NPAR with infection susceptibility and clinical outcomes in *E. coli* BSI.

Data Confidentiality Statement

All patient data were handled in strict compliance with confidentiality regulations. The data were anonymized prior to analysis, and no identifiable personal information was disclosed or shared outside the research team.

Data Sharing Statement

The data are available from the corresponding author on reasonable request.

Consent to Participate

This research was approved and waived the consent by the Ethics Committee of Chinese PLA General Hospital (NO. S2020-25601). Informed consent was not required due to the retrospective nature of the study design. All authors confirm this study adheres to the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors in this study declare no competing conflicts.

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